# EXHIBIT 24

# Expert Report of David Weill, M.D.

In re W.R. Grace & Co., *et al.*

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platinum compounds. A Phase III trial of pemetrexed with cisplatin is underway and may soon establish a standard of care. Raltitrexed combined with oxaliplatin has also been shown to be effective [71] as has gemcitabine when used as a single agent or in combination with cisplatin.

## E. Lung Cancer

The link between lung cancer and asbestos exposure has been known for many years. From a clinical perspective, lung cancer in an asbestos exposed worker is similar to that found in non-exposed people. After the initial report in 1935 by Lynch and Smith of lung cancer in an asbestos worker, there was an additional follow-up case series in the 1940s [72]. First established epidemiologically in a workplace-exposed population by Doll in 1955 [2], debate has subsequently centered on the relative roles of asbestos exposure and cigarette smoking on lung cancer development. The Doll study was followed by the Selikoff paper [73] in 1968 which found an increased cancer risk in insulators who were smokers, as compared to non-asbestos exposed non-smokers. This finding led Selikoff to conclude that there was a multiplicative effect of asbestos exposure and cigarette smoke with regard to cancer risk.

While there is widespread agreement about the role of cigarette smoking in causing lung cancer, the relationship between asbestos exposure, asbestosis, and lung cancer has been intensely debated, both in the academic and legal arenas. The opinions regarding this relationship can be divided into three positions: one, exposure to asbestos of any amount increases the lung cancer risk; two, exposure to asbestos of amounts sufficient to cause asbestosis are necessary to attribute lung cancer to exposure; and, three, asbestosis (either radiographically evident or present on histologic material) is

necessary to attribute lung cancer to asbestos exposure in an individual case. The weight of the scientific evidence favors asbestosis as a necessary precursor in order to attribute lung cancer to asbestos exposure.

Pathogenesis

The role of asbestos in lung cancer development likely involves common biochemical pathways that lead to both fibrosis and carcinogenesis. While initially thought to be "scar carcinomas" (i.e. tumors that arise in a scarred area of lung due to transformation of the fibrotic tissue into cancerous tissue), lung cancers that occur in asbestotics likely do so as a result of molecular pathways that cause damage to DNA, leading either to fibrosis or to cancer development. Of course, whether an individual patient develops fibrosis or cancer or both likely depends on the nature and the extent of the cellular damage. In a clinical study involving the risk of lung cancer in those with cryptogenic (idiopathic) fibrosing alveolitis, Turner-Warwick and colleagues [74] found a risk ratio of 14.2 in male smokers with lung fibrosis not related to a specific cause. This study demonstrated that lung fibrosis, from any cause or without known cause, may be a marker for those with excess cancer risk. Similar studies have shown an excess cancer risk in patients with another fibrosing lung disease (scleroderma) [75, 76]. These studies indicated that there is a lung cancer risk that is not accounted for by age and smoking history.

Other pieces of clinical data supporting the lung fibrosis-lung cancer model include the fact that, while asbestosis leads to predominantly lower lung zone fibrosis, lung cancers associated with asbestosis can be in any lung zone and do not seem to have a predilection for any particular lung zone [77, 78]. Further, while most "scar

carcinomas" are adenocarcinoma cell type, the lung cancers associated with asbestosis can be of essentially any cell type [79] and are indistinguishable from cancers attributable to cigarette smoking [78, 80].

Epidemiology

The question of whether asbestosis needs to be present in order to attribute lung cancer to asbestos exposure continues to be debated, and several studies have been performed to evaluate the asbestos-lung cancer relationship. Despite this, there is disagreement about some fundamental aspects of the asbestos exposure-lung cancer risk. The link between asbestosis and lung cancer has been studied since the 1950s. Proponents of the assertion that asbestosis is necessary point to the original Doll study in 1955 that found that all of the 11 asbestos workers who died of lung cancer also had histological evidence of asbestosis. Further studies of the Quebec miners found that radiographic abnormalities consistent with asbestosis were found in most but not all the excess deaths due to lung cancer [81]. In the Quebec study, however, the chest radiographs used were often taken many years before death, and, therefore, there may not have been an adequate time period in order for fibrosis to become radiographically apparent.

In a necropsy study of 339 amphibole asbestos miners by Sluis-Cremer [82], the presence of asbestosis was significantly associated with the presence of lung cancer. Of the 35 cases of lung cancer, 24 were associated with asbestosis. Eleven cases of bronchial cancer occurred in men without asbestosis; all were smokers. Standardized proportional mortality rates indicated no excess of lung cancer in 302 exposed men without asbestosis. From these data, the authors concluded that in the absence of

histologically proven asbestosis, lung cancer in those exposed to asbestos was unlikely to be attributable to asbestos exposure.

In a study which had detailed radiographic information about an exposed cohort, Hughes performed a prospective mortality study of 839 men employed in the manufacture of asbestos cement products and examined the lung cancer risk in relation to lung fibrosis seen on chest radiographs and controlled for age, smoking, and exposure to asbestos [36]. In a follow-up period that extended more than 20 years after first hire, no excess of lung cancer was found among workers without radiographically detectable lung fibrosis, even among long term workers (greater than or equal to 21.5 years). There was also not a trend toward increased risk by level of cumulative exposure to asbestos among these workers. By contrast, employees with small opacities (greater than or equal to 1/0) experienced a significantly raised risk of lung cancer (nine observed deaths v 2.1 expected), even though their exposures to asbestos were similar to the exposures of long term workers without opacities. The authors concluded that excess risk of lung cancer was restricted to workers with chest radiographic evidence of asbestosis.

Other data suggests that the lung cancer risk is linearly related to dose and not to the presences or absence of asbestosis. For example, Wilkinson examined occupational and smoking data from 271 patients with a confirmed diagnosis of primary lung cancer and 678 controls from a hospital specializing in chest diseases [83]. To allow for adequate latency, workers were classified by the time they had spent in an occupation and assigned an exposure category (definite or probable) more than 15 years before diagnosis. Chest radiographs were interpreted by three readers and scored for small opacities. After adjustment for age, sex, smoking history, and area of referral, the odds ratio was 2.03 in

the subgroup of 211 with a median ILO score for small parenchymal opacities of 1/0 or more, and 1.56 (1.02-2.39) in the 738 with a score of 0/1 or less (i.e. those without radiological evidence of pulmonary fibrosis). The authors concluded that these data suggested that asbestos is associated with lung cancer even in the absence of radiographically apparent pulmonary fibrosis. Of course, limitations of the study include the accuracy of exposure estimates, the possibility of misinterpreting the chest radiographs when portions of the radiographs are blocked out (and one is unable to exclude other diseases that cause small opacities), and the absence of relationship between years of exposure and lung cancer risk particularly in those with normal (i.e. ILO 0/0) radiographs and sufficient latency. Further, the use of controls from a hospital population that is defined by the presence of chest disease is problematic.

Some studies have indicated that there is a dose-response relationship between asbestos exposure and lung cancer risk, even at low levels of exposure [84]. However, in his meta-analysis of asbestos-exposed lung cancer cohorts, Weiss found a high correlation between asbestosis rates and lung cancer rates in 38 cohorts, but a poor correlation between cumulative exposure data and lung cancer relative risks in the eight cohorts with adequate data [85]. One area of agreement, however, is that the latency period for lung cancer is generally shorter than that for mesothelioma and is likely greater than 15 years [86] but may be as long as 40 years [87].

Although no epidemiologic study is without flaws, the least confounded studies demonstrate that excess lung cancer risk was found only in those with radiographic or histologically demonstrated asbestosis [36, 82]. In the instance of the Hughes study, the prospective cohort design was more powerful in answering the causation question than

case-control or fiber burden studies. Further, in the studies that suggested that a synergy existed between asbestos exposure, cigarette smoking, and lung cancer risk, there was no distinction made between those with and without either radiographic or histologic asbestosis. If the cohort studies that identify the presence or absences of asbestosis are given the most weight in assessing lung cancer risk, the synergism would likely exist between *asbestosis* and cigarette smoking, rather than between asbestos exposure and cigarette smoking as first suggested by Selikoff. Therefore, while the weight of the scientific evidence favors asbestosis as a necessary precursor in order to diagnose an asbestos-attributable lung cancer [36, 85], not all have accepted this premise [83] and the issue will continue to be debated, particularly in matters of compensation.

# III. Diagnosis of Asbestos-Related Lung Disease

## A. Diagnosis of Asbestosis

Because histopathology is often not available in suspected cases of asbestosis, the diagnosis of this disease usually is based on clinical parameters alone. When pathologic material is available, a diagnosis of asbestosis is established when both asbestos bodies and fibrosis are present. Neither of these alone is sufficient in establishing a pathologic diagnosis. The diagnosis of asbestosis is usually based on clinical parameters and was described in an American Thoracic Society statement from 1986 [88].

In the Statement, the Committee recognized that pathologic material was rarely available in order to confirm a diagnosis of asbestosis but that the hallmark of asbestosis histopathologically was the demonstration of asbestos bodies in the presence of interstitial fibrosis. The authors of the Statement also commented that asbestos bodies